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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/017,717	12/14/2001	Guy Michael Miller	346392001500	5287

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EXAMINER	
SPIVACK, PHYLLIS G	

ART UNIT	PAPER NUMBER
1614	

DATE MAILED: 08/14/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
10/017,717	Miller et al.
Examiner	**Art Unit**
Phyllis G. Spivack	1614

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☐ Responsive to communication(s) filed on _____.

2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) 1-97 is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) 1-97 is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 4,5,6
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

Upon reconsideration the request for an election of species is withdrawn. Claims 1-97 are presented and represent all of the claims under consideration.

Information Disclosure Statements filed September 3, 2002, November 6, 2002 and December 10, 2002, Paper Nos. 4, 5 and 6, respectively, are acknowledged. Each has been reviewed to the extent references have been provided or were readily obtainable.

Claims 65-69, 76-81, 85, 87 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention.

Claim 65 is indefinite and lacks clarity because the metes and bounds of the recitation "a flavonoid and/or a flavonoid derivative" cannot be precisely determined. Applicants should recite those derivatives contemplated.

Claims 85 and 87 recite the limitation "metabolite". There is insufficient antecedent basis for this limitation in claim 82 from which the claims depend.

Claims 3, 5, 7, 8, 24-32, 39-41 and 48-50 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the administration of gamma, beta, delta tocopherols and the single metabolite gamma-CEHC to treat ischemia, does not reasonably provide enablement for any metabolite of gamma, delta or beta tocopherol, or any flavonoid, in the treatment of ischemic conditions. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims. The claims are directed to a treatment or amelioration

of a tissue ischemic condition condition comprising administering a non-alpha tocopherol, a metabolite thereof, or a flavonoid. The specification provides support for countering ischemia comprising administering gamma-, delta-, beta-tocopherol or the single metabolite gamma-CEHC. It is noted the generic term "flavonoid" is used in the assessment of cell viability in Figure 7.

Attention is directed to In re Wands, 8 USPQ2d 1400 where the court set forth factors to consider when assessing whether or not a disclosure would require undue experimentation. These factors are:

1) the quantity of experimentation necessary

2) the amount of direction or guidance provided

3) the presence or absence of working examples

4) the nature of the invention

5) the state of the art

6) the relative skill of those in the art

7) the predictability of the art and

8) the breadth of the claims.

The instant specification fails to provide guidance that would allow the skilled artisan background sufficient to practice the instant invention without resorting to undue experimentation in view of further discussion below.

The nature of the invention, state of the prior art, relative skill of those in the art and the predictability of the art

The claimed invention relates to treatment of various ischemic conditions.

The relative skill of those in the art is generally that of a Ph.D or M.D.

Each particular ischemic disease or condition has its own specific characteristics and etiology. The broad recitations "metabolite" of a particular tocopherol and "flavonoid" are inclusive of many structurally distinct compounds that have no support in the specification for the claimed methods of use.

It is clear the art to which the present invention relates is highly unpredictable and unreliable with respect to conclusions drawn from laboratory data extrapolated to clinical efficacy.

The breadth of the claims

The claims are very broad and inclusive of any metabolite of gamma, beta and delta tocopherol and various flavonoids and/or flavonoid derivatives for use in treating and/or ameliorating ischemic conditions.

The amount of direction or guidance provided and the presence or absence of working examples

The working examples are limited to the administration of gamma-, beta-, and delta-tocopherol, and the one metabolite, gamma-CEHC. Figure 7 discloses the results of administering an unspecified flavonoid with ferric ions to decrease cell death.

The quantity of experimentation necessary

Applicants have failed to provide guidance as to which particular metabolites and flavonoids would be preferred for treatment of the many types of ischemia that are recited in the

claims. The skilled artisan would expect the mechanism of action of a specific metabolite in the treatment of a particular condition to be very specific and highly unpredictable absent a clear understanding of the structural and biochemical basis for each agent. The instant specification sets forth no such understanding nor any criteria for extrapolating beyond the single disclosed metabolite and an unspecified flavonoid. No direction is provided to administer any other metabolite in addition to gamma-CEHC. Absent a reasonable *a priori* expectation of success for using a particular metabolite or flavonoid to treat ischemia, one skilled in the art would have to test extensively many metabolites and flavonoids to discover which one is effective in treatment. Since each prospective embodiment, as well as future embodiments as the art progresses, would have to be empirically tested, undue experimentation would be required to practice the invention as it is claimed in its current scope. The specification provides inadequate guidance to do otherwise.

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 C FR 1.321© may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 C FR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 C FR 3.73(b).

Claims 1-64 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-62 of copending Application No. 10/020450. Although the conflicting claims are not identical, they are not patentably distinct from each other because of overlapping subject matter.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 41-64 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wechter, W.J., WO 00/35444.

Wechter teaches the administration of gamma tocopherol and a metabolite, LLU-α, in the treatment of ineffective renal perfusion, a noncardiovascular tissue ischemic condition. Renal ischemia is included among those non-cardiovascular ischemic conditions recited in claim 43. See page 3, line 29. Various concentrations of γ-tocopherol and the LLU-α metabolite, as required by claims 44-57, and oral formulations are disclosed on page 20. As required by claims 62-64, a total daily dose is taught on page 21, line 23. Nutritional compositions comprising gamma-tocopherol are established in the prior art. The claims differ in that Wechter's teaching broadly discloses multiple disease states involving different organ systems such as cancer, neuropathologies and immunologic deficits. However, one skilled in the nephrology art would have been motivated to administer gamma-tocopherol or a derivative of gamma-tocopherol to treat renal ischemia. Such would have been obvious in the absence of evidence to the contrary because ineffective renal perfusion is inadequate blood flow from the renal artery through the vascular bed of renal tissues.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(e) the invention was described in (1) an application for patent, published under section 122(B), by another in the United States before the invention by Applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the Applicant for patent, except that an international application filed under the treaty defined in

section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-7, 14-27, 34-43 and 58-97 are rejected under 35 U.S.C. 102(e) as being anticipated by Brown et al., U.S. Patent 6,528,042.

Brown teaches the administration of beta-, delta- and gamma-tocopherols and derivatives thereof, which are characterized by a 6-chromanol ring structure and a side chain at the 2-position, for use in the treatment of various ischemic conditions. It would have been reasonable to include metabolites in Brown's teaching of derivatives. See columns 9, line 63, to column 10, line 22; column 10, line 1, to column 11, line 10; and column 13, lines 21-35. Further, Brown teaches the administration of various flavonoids in the treatment of ischemic conditions. See column 5, lines 50-52, column 14, lines 30-67, and column 30, lines 66-67. As required by claim 82, combinations of active ingredients are disclosed in column 8, lines 43-44, and column 49, line 55, to column 50, line 34. Mixtures of flavonoids and tocopherols are disclosed in Example 11, column 49. Various compositions, including nutritional formulations, are disclosed in column 24, lines 46-54, and column 26, lines 20-24.

No claim is allowed.

Any inquiry concerning this communication should be directed to Phyllis Spivack at telephone number 703-308-4703.

August 10, 2003

Phyllis Spivack

PHYLLIS SPIVACK
PRIMARY EXAMINER